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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/005,467	12/04/2001	Keith D. Allen	R-758	7217

26619 7590 03/22/2005

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EXAMINER	
QIAN, CELINE X	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 03/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/005,467	ALLEN, KEITH D.	
	Examiner	Art Unit	
	Celine X. Qian Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-32,37,47 and 52-58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-32,37,47 and 52-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 28-32, 37, 47, 52-58 are pending in the application.

This Office Action is in response to the Amendment filed on 2/17/05.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/17/05 has been entered.

Response to Amendment

Claims 28-32, 37, 47, 52-58 are rejected under 35 U.S.C.101/112 1st paragraph for reasons discussed below.

Claims 28-32, 37, 47, 52-54, 57 are rejected under 35 U.S.C.112 1st paragraph (new matter) for reasons discussed below.

Claim 32 is rejected under 35 U.S.C.112 2nd paragraph for reasons given below.

New Grounds of Rejection

Claim Rejections - 35 USC § 101

Claims 28-32, 37, 47, 52-58 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, substantial and specific asserted utility or a well established utility.

The claims are drawn to a transgenic mouse whose genome comprises a null endogenous PTP36 allele, wherein the null allele comprises exogenous DNA, wherein the mouse is

heterozygous for said null allele, the transgenic mouse exhibits, relative to a wild type mouse, uterine abnormality comprising keratin in the uterine horn or lumen, increased organ weight. The claims are further drawn to a cell or tissue isolated from said mouse and a method for producing said mouse.

No well-established utility exists for the claimed transgenic mouse. However, the specification asserts or implies the following as credible, specific and substantial patentable utilities for the claimed transgenic knockout mouse and cells or tissues isolated from said mouse:

1) To be used in methods of identifying agents capable of affecting a phenotype of said mouse.

2) To identify agents useful as therapeutic agents for treating conditions associated with a disruption or other mutation of the PTP36 gene.

3) To identify agents having an effect on PTP36 expression or function.

4) To serve as models for diseases.

5) To test and develop new treatments relating to the behavioral phenotypes.

Each of the following shall be addressed in turn:

1) To be used in methods of identifying agents capable of affecting a phenotype of said mouse. This utility is not credible, substantial and specific because the specification does not disclose a utility for such agents. The phenotype of uterine abnormality comprising keratin in the uterine horn or lumen, increased organ weight is resulted from the disruption of a single gene PTP36, however, such genotypic-phenotypic association is not known in the art for relating to a specific disease. Although the agents can affect a phenotype in said transgenic mouse or a cell/tissue isolated from said mouse, the utility is not substantial because there is no other use of

said agents except affecting a phenotype only exists in a mouse model. Since this asserted utility is not presented in mature form so it could be readily used in a real world sense, the asserted utility is not credible, substantial and specific.

2) To identify agents useful as therapeutic agents for treating conditions associated with a disruption or other mutation of the PTP36 gene. This utility is not credible, specific and substantial because the specification does not disclose what kind of conditions is associated with a disruption or other mutations of the PTP36gene. The specification also fails to teach what specific condition is associated with the overall of phenotype uterine abnormality comprising keratin in the uterine horn or lumen, increased organ weight. The art does not recognize any disorders that are associated with the overall phenotype of increased organ weight, keratin in the uterine horn and lumen. As such, the claimed mouse is not a valid model for any disorder. Since this asserted utility is not presented in mature form so it could be readily used in a real world sense, the asserted utility is not credible, specific and substantial.

3) To identify agents having an effect on PTP36 expression or function. This asserted utility is not credible, substantial and specific because the specification does not disclose 1) how to use a mouse or cell that does not express PTP36 to identify agents which affect the gene expression or function; 2) how to use such identified agents that affect PTP36 expression or function. Since the identified agents does not have a substantial utility, the claimed mouse or mouse cells used in a method for identifying such agents does not have substantial utility as well. This asserted utility is not credible since there is no expression or function can be monitored in the knockout mouse or cells/tissues isolated from said mouse, it is unclear how these agents that affect PTP36 expression/function can be identified.

4) To serve as models for diseases. The asserted utility is not credible, substantial and specific because the specification does not disclose what types of disease the transgenic mouse or cells/tissues isolated from said mouse represents (see discussion in 2).

5) To test and develop new treatments relating to the behavioral phenotypes. This utility is not credible, substantial and specific because the claimed mouse does not display any behavioral abnormality. As such, it is not a valid model for any behavioral disorder. Since this asserted utility is not presented in mature form so it could be readily used in a real world sense, the asserted utility is not credible, specific or substantial.

Since the claimed transgenic mouse and cells/tissues isolated from said mouse does not have utility, the method for producing said transgenic mouse does not have utility either. Therefore, the claimed invention lacks patentable utility for reasons given above.

Claims 28-32; 37, 47, 52-58 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible, substantial and specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. (see also the reasons set forth in the office action mailed on 4/23/04 and 12/16/04).

In response to the 112 1st rejection raised in the previous office actions, Applicant asserts that the following arguments is based on the assumption that the rejection is 101/112 1st paragraph. Applicant argues that the newly amended claim 28, drawn to a transgenic mouse having one PTP36 null allele which comprises exogenous DNA, has patentable utility according to utility guidelines set forth in MPEP because the claimed invention has a well-established

utility. Applicant assert that the skilled in the art would immediately appreciate how to use a knockout mouse because any knockout mouse has the inherent and well-established utility of defining the function and role of the disrupted gene regardless of specific phenotypes, characterizations or properties of the knockout mouse. Applicant further cites a passage at NIH website which indicate that knockout mice represent a critical tool in studying gene function. Furthermore, Applicant asserts that the newly amended claims drawn to transgenic mouse comprising null-reporter alleles "is an indispensable starting point for studying the function of every gene"(Austin et al., 2004), "is an invaluable tool for investigating gene function on a genomic scale"(Molecular biology of Cell, Albert, 4th ed., Garland Science (2002), "is a powerful tool to investigate directly the importance and function of the gene" (Genes VII, Oxford university 2000), "offers a powerful approach to study gene function in a mammalian organism," (Joyner, Gene targeting: A Practical Approach, Oxford University Press 2000), "has revolutionized our ability to study gene function in cell culture *in vivo*," (Matise, Production of Targeted Embryonic Stem Cell Clones), and "provide an important means for understanding gene function."(Crawley, what's wrong with my mouse behavioral phenotype of transgenic and knockout mice, Wiley-Liss 2000). Moreover, Applicant asserts that the knockout mouse have a clear, specific and unquestionable utility as with gas chromatographs, screening assays and nucleotide sequence techniques as taught by MPEP 2107.01,I. Furthermore, Applicant also asserts that the claimed invention is useful for a particular purpose since the mouse has specific disclosed phenotype. As such, the utility of the claimed mouse is apparent to one of skilled in the art as the role of the knockout mouse in studying such phenotype. Moreover, Applicant argues that the utility of the claimed inventions does not depend on a correlation between the

disclosed phenotype and a disease in human according to *In re Brana*, and the knockout mouse with a specific gene disrupted is a widely accepted model for determine gene function (Austin and Doetschman) with well-established utility. Moreover, Applicant argues that the claimed mouse have specific utility. Applicant asserts that use of GAL1R-/+ mouse to study the function of the GAL1R gene and the association of the GAL1R gene with the development of the female sex organ is specific to this mouse. Applicant further asserts that no further research is required to identify any utility for the instant claimed mouse. Applicant asserts that Applicant has determined that the GRL1R gene is associated with sex organ development, which is an immediate benefit to the public. Applicant assert that whether additional research is required to identify drugs capable of targeting the GRL1R receptor or gene or further investigate the function of the gene is irrelevant to whether the claimed invention has satisfied utility requirement according to MPEP utility guideline. Further, Applicant asserts that the examiner has effectively admitted that one of ordinary skilled in the art would know how to make and use the claimed invention based on a previous 103 (a) rejection, thus it would be contradictory to argue that one of ordinary skill would have been motivated to make and use a knockout mouse but then argue such a mouse once created would not meet the utility requirement. Applicant again argues that the legal principles and facts of *In re Brana* are applicable to the instant case. Applicant assert that a mouse demonstrating sex organ abnormality and growth abnormality is sufficient to establish an animal's use as a model of a disease or condition, wherein confirmation of the phenotype in human is unnecessary. In addition, Applicant asserts that the claimed mouse can be used to study gene expression since the null allele comprises a visible marker. Applicant thus concludes that the claimed invention has credible, substantial and specific utility.

These arguments have been fully considered but deemed unpersuasive. The reasons for the utility and non-enablement rejection were discussed in detail in the office action mailed on 12/16/04 and in the utility rejection discussed above. In response to Applicant's response regarding any knockout mouse has a well-established utility, the examiner does not agree with Applicant's assertion that the claimed invention has a well-established utility. Applicant is reminded that in MPEP, the guideline for the utility requirement clearly states: "An invention has a well-established utility if (i) a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention (e.g., properties or applications of a product or process), and (ii) the utility is specific, substantial, and credible." In the instant case, the utility that applies to any knockout mouse is not specific to the claimed invention, the PTP36 transgenic mouse having a heterozygous null allele. It was well known to knock out a gene to determine its function or what will happen when the gene is not expressed. However, scientific "utility" is not the same as "patentable utility" or a "well-established" utility, of which must be specific, substantial and credible. At the time of filing, knockout mice were used for further research in the art as indicated by the quotations cited by Applicant, for example, studying gene function. However, further research does not rise to the level of a "well-established utility" because such a utility is not substantial. The utility guidelines specifically state that further research is not a "substantial utility." The MPEP states "the following are examples of situations that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use and, therefore, do not define "substantial utilities": A. Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved..." In this case, further study of mice would have

been required to determine how to use the mouse of applicant's invention according to the embodiments described in the specification. Applicant's assertion that the claimed mouse is useful to study the function of PTP36 is an invitation for further research on the claimed invention in which the function of said invention Applicant clearly does not know. Further study would be required to determine the function of the disrupted gene. Furthermore, the overall phenotype of the claimed mice does not correlate to any disorder; therefore, further study would be required to determine how to use the mice to study a disorder, screening drugs and treatment for such disorder. Thus, using the mice claimed for further research is not a "substantial utility."

Similarly, using the mouse comprising null-reporter to study gene expression is not a patentable utility because it is not a substantial and specific utility for the instant claimed mouse, which is a transgenic mouse comprising a null PTP36 allele. Studying the expression of a gene in which the function is unknown is not a substantial utility, whereas studying the expression of a gene using null-reporter is not a specific utility to the mouse comprising a null PTP36 allele.

In response to Applicant's argument with regard to the specific phenotype, as discussed in the previous office action and above, the overall phenotype of increased organ weight and keratin in uterine horn and lumen disclosed by the instant specification does not correlate with any known disease (either mouse or human). As such, it is not apparent to one of ordinary skilled in the art to immediately appreciate how to use the claimed mouse base on such characteristics. The specification fails to teach how to use the claimed mouse according to its overall characteristics because the utility disclosed in the specification is not credible, substantial and specific for reasons discussed in the previous office action. Therefore, the specification does not provide enough information

for use the claimed mouse as a valid model for any type of disorders. The examiner cannot comment of the use of GAL1R-/+ mouse to study the function of the GAL1R gene and the association of the GAL1R gene with the development of the female sex organ because the specification does not teach a GAL1R-/+ mouse; and the examiner fails to recognize the relationship between the PTP36 knockout mouse and the GAL1R-/+ mouse. However, the examiner reiterate the position that further study of mice would have been required to determine how to use the mouse of applicant's invention according to the embodiments described in the specification. Contrary to Applicant's assertion, using the mice to identify the function of the knocked out gene is not a "substantial utility" or "specific utility." Olsen (GABA in the Nervous System, 2000, pg 81-95) taught that "although gene targeting is often useful in delineating the contribution of a given gene product to phenotypic characteristics observed, some gene knockouts lead to embryonic or perinatal lethality, and others lead to no apparent phenotype. This can arise from a lack of any role for the gene in question in regard to the trait studies or from compensation by other gene products. Analysis of the compensation can yield valuable clues to the genetic pathway" (pg 82, last 11 lines of col. 1). Thus, knockout mice may not be capable of elucidating the function of the protein and may only provide a clue to a pathway the protein being knocked out is involved in. Using mice to obtain a clue to a pathway is not a "substantial utility." Using a mouse with a phenotype caused by genes compensating for a knocked out gene is not a "specific utility" because the phenotype is not specific to the knocked out gene.

In response to Applicant's argument regard *In re Brana*, the examiner maintains the position that it does not applies in the instant case. Although the case law states "Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development," it is referring to a chemical compound for its anti-tumor activity which has been demonstrated in tumor cell line. The specification of that application has taught a substantial and specific use for the claimed compound. However, in the instant case, the claimed knockout mouse does not have a credible, substantial and specific use since the specification does not teach credibly what disease model the claimed mouse represents and/or what type of drug the claimed mouse can screen. The utility of using the claimed mouse to study PTP36 function is not credible, substantial and specific because the function of the PTP36 is unknown. Furthermore, as discussed in the previous office action and above, the claimed mouse is not a valid model for any disorder. As such, the utility of seeking treatment for unknown disorder is not credible, substantial and specific. Moreover, as discussed above, the utility of studying the function of the PTP36 gene is an invitation of further research in which the function of the claimed invention is not known. Similarly, studying the expression of a gene of which the function is unknown is not a credible, substantial and specific utility for the claimed mouse. The examiner would also like to point out that the specification does not demonstrate an animal having sex organ abnormality, as such, the argument of such animal having public benefit is irrelevant to the instant rejection.

In response to Applicant's argument regard previous 103 rejection, Applicant is reminded that the rejection does not apply to any of the pending claims, it was applied to a different invention. As such, the motivation for making a different invention or an invention of different scope neither give the current claimed invention a patentable utility nor how to use it (to satisfy both 101 and 112 1st paragraph) because it is directed to a different invention and such motivation can be for research use. Therefore, there is no contradiction in examiner's position on the currently claimed invention.

For reasons given in the previous office action and above, the specification fails to disclose a credible, substantial and specific use for the claimed mouse and one skilled in the art would not know how to use the claimed mouse according to the embodiments disclosed by the instant specification. Since the claimed mouse does not have patentable utility, the method of making the mouse also lacks patentable utility. The rejection is thus maintained.

Newly added claims 53-58 are rejected for same reasons as set forth in the office action mailed on 12/16/04 and discussed above.

In response to the 112 1st paragraph rejection, Applicant presents the same reasons as discussed above.

For same reasons set forth in the previous office actions and above, the 112 1st rejection is maintained.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 28-32, 37, 47, 52-54, 57 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The amended claims are drawn to a mouse whose genome comprises a null PTP36 allele, wherein said null allele comprises exogenous DNA. The claim is further drawn to such a mouse wherein it comprises a null PTP36 allele comprises exogenous DNA that comprises a visible marker (claim 57). The original specification does not disclose a knockout mouse comprises a null allele that comprises an exogenous DNA or a visible marker. The disclosure of a selection marker is not sufficient to support the genus of "a null allele comprise exogenous DNA," whereas the disclosure of a single lacZ gene is not sufficient to support the claimed genus of "a gene encoding a visible marker." The specification fails to provide sufficient written description support for this limitation. Therefore, such recitation constitutes new matter.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 32 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of "increased thymus weight increased liver weight relative to body weight and increased spleen weight relative to body weight" is confusing because it is unclear what weight is increased. Applicant is advised to use comma to separate each weight so that the metes and bounds of the claim can be determined.

Correction to 112 2nd rejection.

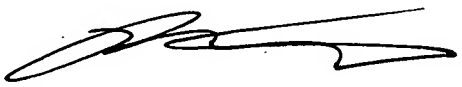
The Examiner would like to clarify that 112 2nd is not applied to claim 52.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X. Qian Ph.D. whose telephone number is 571-272-0777. The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Celine X Qian Ph.D.
Examiner
Art Unit 1636



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